REMARKS

Reconsideration and allowance are respectfully requested.

Claims 30-32 are pending. Rejections against claims 27-29 are rendered moot by their cancellation.

The amendments are supported by the original disclosure and, thus, no new matter has been added. The limitations recited in claims 27-29 have been incorporated in independent claims 30-32.

35 U.S.C. 112 – Definiteness

Claims 30-32 were rejected under Section 112, second paragraph, as being allegedly "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." The Action stated on page 2 that "it is not clear what present in the milligram amounts means, as a composition comprises a concentration of a particular item, such as grams/liter, for example" (Paper No. 8). Applicants traverse.

"If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, §112 demands no more." Miles Laboratories, Inc. v. Shandon Inc., 997 F.2d 870, 875, 27 USPQ2d 1123, ___ (Fed. Cir. 1993), *citing* Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1375, 231 USPQ 81, 87 (Fed. Cir. 1986), *cert. denied,* 480 U.S. 947, 94 L.Ed.2d 792, 107 S.Ct. 1606 (1987). The rejected claims are directed to a pharmaceutical composition in which from 0.1 mg to 6 g of the recited globin chain is present in the composition, regardless of the concentration. There is no ambiguity as to whether a given composition is included or excluded from the claim and no reason has been given as to why the person of skill in the art would not understand the scope of the claim. Rather, the rejection appears to be based on the assertion that the recitation of amounts is not permitted in claims directed to compositions. No authority or reason has been given for such assertion.

Claims 27-29 did not recite a concentration and were not included in the rejection. Therefore, applicants understand the basis of the rejection to be the recitation of an amount in claims 30-32 and not the failure to recite a concentration.

Applicants request withdrawal of the Section 112, second paragraph, rejection because the pending claims are clear and definite.

35 U.S.C. 102 – Novelty

To be anticipated under Section 102, each and every element of a claim must be disclosed, either explicitly or inherently, in a single reference. Lewmar Marine, Inc., v. Barient, Inc., 827 F.2d 744, 747, 3 USPQ2d 1766, ___ (Fed. Cir. 1987). "Inherency, however, may not be established by probabilities or possibilities." Continental Can Co. v. Monsanto Co. 948 F 2d 1264. 1269. 20 USPQ2d 1746. ___ (Fed Cir 1991) *quoting,* In re Oelrich, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981). The burden is on the PTO to cite evidence that the allegedly inherent limitation is necessarily present in the prior art reference, not on applicant to prove otherwise. In re Robertson, 169 F.3d 743, 745, 49 USPQ2d 1949, ___ (Fed. Cir. 1999).

Moreover, the mere fact that the teaching of the prior art can be modified to arrive at a claimed invention is insufficient to establish obviousness. In re Gordon, 733 F.2d 900, 902, 221 USPQ 1125, ___ (Fed. Cir. 1984). Since "lack of novelty is the ultimate of obviousness" (In re Fracalossi, 681, F.2d 792, 794, 215 USPQ 569, ___ (CCPA 1982)), it therefore follows that the mere fact that the teaching of the prior art can be modified to arrive at a claimed invention is insufficient to establish anticipation.

Because each of the anticipation rejections violates the preceding principles as discussed below, the rejections are improper and should be withdrawn.

Claims 27-32 were rejected under Section 102(b) as allegedly being anticipated by Tame et al. (J. Mol. Biol. 218:761-767, 1991). Applicants traverse for three different reasons. The first is by itself sufficient to overcome the rejection of claim 31, the second is by itself sufficient to overcome the rejection of claim 32, and the third is by itself sufficient to overcome the rejection of claims 30-32.

Claim 31 is directed to a pharmaceutical composition consisting essentially of the beta-globin chain of hemoglobin in a pharmaceutically acceptable carrier, wherein the composition is suitable for subcutaneous administration and wherein the beta-globin chain is present in an amount of 0.1 mg to 6 g. It is undisputed that Tame et al. do not

disclose whether the beta globin disclosed therein was in a pharmaceutically acceptable carrier. Instead, the rejection is impermissibly based on an assumption as to how the beta-globin solution was made. Thus, the Action states on page 2, "Claim 28 is included in this rejection because the β-globin added to the α-globin was most likely in the same buffer as the α-globin because it was added in 'molar excess'" (emphasis added, Paper No. 8). (Although the above-quoted passage from the Office Action referred to claim 28, the reasoning therein would appear to be equally applicable to claim 31 because claim 31 depended from claim 28.) The rejection of claim 31 as allegedly being anticipated by Tame et al cannot be maintained because an anticipation rejection cannot be based on probabilities or possibilities. Robertson ("the allegedly inherent limitation is necessarily present in the prior art reference").

Claim 32 is directed to a pharmaceutical composition consisting of the alpha-globin chain of hemoglobin and the beta-globin chain of hemoglobin in a pharmaceutically acceptable carrier, wherein the composition is suitable for subcutaneous administration and wherein the beta-globin chain and the alpha-globin chain are each present in an amount of 0.1 mg to 6 g. The Action on page 2 cites Tame et al. as teaching that "β-globin was added to the α-globin solution in the presence of hemin dicyanide" (Paper No. 8). Tame et al. do not disclose whether the resulting solution containing both alpha- and beta-globin was pharmaceutically acceptable. Indeed the added β-globin is the same β-globin that the PTO asserts to have "most likely" been in the same buffer as the α-globin solution to which it was added. Since the composition of the β-globin added is not disclosed, it cannot be inferred that the carrier that resulted from the mixture of the two solutions was pharmaceutically acceptable. Again, an anticipation rejection cannot be based on possibilities or probabilities because the allegedly inherent limitation must be disclosed in the prior art reference. Robertson.

Claims 30-32 are directed to pharmaceutical compositions consisting essentially of a single or both globin chains of hemoglobin in a pharmaceutically acceptable carrier, wherein the composition is suitable for subcutaneous administration and the recited globin chain(s) is present in an amount of 0.1 mg to 6 g. It is undisputed that Tame et al.

do not disclose a composition containing the recited amount of any globin chain. Instead, the rejection is impermissibly based on what could be made. Thus, the Action states on page 3, "Claims 30 to 32 are included in this rejection because there is no concentration provided in the claims, and enough of the solutions taught in Tame et al. et al. can be made to comprise 0.1 mg to 6 g of globin" (emphasis added, Paper No. 8). But that is not sufficient to maintain the rejection since in anticipation the issue is not what can be made, but what was made or disclosed. Tame et al. do not disclose the making of a solution containing from 0.1 mg to 6 g of alpha globin and/or beta globin. Therefore, Tame et al. do not disclose each and every element of claims 30-32

Claims 29 and 32 were rejected under Section 102(e) as allegedly being anticipated by Estep (U.S. Patent 4,861,867). Applicants traverse for two different reasons, either of which by itself is sufficient to overcome the rejection.

Claim 32 is directed to a pharmaceutical composition consisting of the alpha globin chain of hemoglobin and the beta globin chain of hemoglobin in a pharmaceutically acceptable carrier, wherein the composition is suitable for subcutaneous administration. The Action stated on page 3, "Estep teaches hemoglobin in phosphate buffer solution . . . . [t]herefore, compositions comprising α- and β-globin is anticipated by Estep" (Paper No. 8). Hemoglobin contains alpha- and beta-globin chains, as well as containing heme groups. The "consisting of" transition in claim 32 explicitly excludes a heme group. Therefore claim 32 does not read on the hemoglobin taught by Estep.

Claim 32 recites that the alpha- and beta-globin chains are each present in an amount of 0.1 mg to 6 g. It is undisputed that Estep does not disclose a composition containing the recited amounts of the alpha- and beta-globin chains. Instead, the rejection is impermissibly based on what could be made following the teaching of Estep. Thus, the Action states on page 3, "Claim 32 is included in this rejection because there is no concentration provided in the claims, and enough of the solutions taught in Estep can be made to comprise 0.1 mg to 6 g of globin" (emphasis added, Paper No. 8). But that is not sufficient to maintain the rejection since in anticipation the issue is not what can be made, but what was made or disclosed. Estep does not disclose the making of a

solution containing from 0.1 mg to 6 g of alpha-globin and beta-globin. Therefore Estep does not disclose each and every element of claims 30-32.

Claims 27-32 were rejected under Section 102(e) as allegedly being anticipated by Hoffman et al. (U.S. Patent 5,449,759). Applicants traverse for two different reasons, either of which by itself is sufficient to overcome the rejection.

Claims 30-32 are directed to pharmaceutical compositions consisting essentially of the recited globin chains of hemoglobin in a pharmaceutically acceptable carrier, wherein the composition is suitable for subcutaneous administration and wherein the recited globin chain is present in an amount of 0.1 mg to 6 g. It is undisputed that Hoffman et al. do not disclose a composition containing the recited amount of any globin chain. Instead, the rejection is impermissibly based on what could be made. Thus, the Action states on page 3, "Claims 30 to 32 are included in this rejection because there is no concentration provided in the claims, and enough of the solutions taught in Tame [sic, Hoffman] et al. can be made to comprise 0.1 mg to 6 g of globin" (emphasis added, Paper No. 8). But that is not sufficient to maintain the rejection since in anticipation the issue is not what can be made, but what was made or disclosed. Hoffman et al. do not disclose the making of a solution containing from 0.1 mg to 6 g of alpha-globin or beta-globin. Therefore Hoffman et al. do not disclose each and every element of claims 30-32.

As an additional reason for the rejection, the Action stated on page 3, "Example 3 teaches 60 g/l of hemoglobin, which is comprised of α- and α-globin [sic] in a physiologically acceptable blood substitute solution." (Paper No. 8). Hemoglobin contains alpha- and beta-globin chains and also contains heme groups. The "consisting of" transition in claim 32 explicitly excludes a heme group. Therefore claim 32 does not read on the hemoglobin taught by Hoffman et al. Claims 30 and 31 are directed to certain compositions consisting essentially of the alpha-globin chain (claim 30) or the beta-globin chain (claim 31) in a pharmaceutically acceptable carrier. Therefore neither claim 30 nor claim 31 reads on a composition containing both the alpha- and beta-chains.

Withdrawal of the Section 102 rejections is requested because all limitations of the claimed invention are not disclosed by the cited references.

Conclusion

Having fully responded to all of the pending objections and rejections contained in the Office Action (Paper No. 8), Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if any further information is required.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: _____

Gary R. Tanigawa
Reg. No. 43,180

1100 North Glebe Road, 8th Floor
Arlington, VA 22201-4714
Telephone: (703) 816-4000
Facsimile: (703) 816-4100

APPENDIX
MARKED-UP VERSION TO SHOW CHANGES

IN THE CLAIMS

The claims are amended as follows.

30. (Amended) A pharmaceutical composition consisting essentially of the alpha globin chain of hemoglobin in a pharmaceutically acceptable carrier, wherein the composition is suitable for subcutaneous administration and [as in claim 27] said alpha globin chain is present in an amount of 0.1 mg to 6 g.

31. (Amended) A pharmaceutical composition consisting essentially of the beta globin chain of hemoglobin in a pharmaceutically acceptable carrier, wherein the composition is suitable for subcutaneous administration and [as in claim 28] said beta globin chain is present in an amount of 0.1 mg to 6 g.

32. (Amended) A pharmaceutical composition consisting of the alpha globin chain of hemoglobin and the beta globin chain of hemoglobin in a pharmaceutically acceptable carrier, wherein the composition is suitable for subcutaneous administration and [as in claim 29] said beta globin chain and said alpha globin chain are each present in an amount of 0.1 mg to 6 g.

Claims 27-29 are canceled without prejudice or disclaimer.